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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,581	09/05/2006	Yassar Hassan Atef Abdel-Wahab	U0003/7017	5514

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EXAMINER	
CHANDRA, GYAN	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
11/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,581	ABDEL-WAHAB ET AL.	
	Examiner	Art Unit	
	GYAN CHANDRA	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-38* is/are pending in the application.

4a) Of the above claim(s) *15-19,24-28 and 30-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-14,20-23 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/14/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II (claims 10-27 and 29) and election of SEQ ID NO: 3 in the reply filed on 10/14/2008 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, And/Or Claims

Claims 10-38 are pending.

Claims 15-19, 24-28, 30-38 are withdrawn from further consideration as being drawn to a nonelected Invention.

Claims 10-14, 20-23, and 29 are under examination to the extent that they read on elect sequence (i.e., SEQ ID NO: 3).

Specification

Applicants' amendment filed on 5/17/2006 to insert the priority information and SEQ ID Numbers against peptide have been made of record.

Information Disclosure Statement

The Information Disclosure Statement (IDS) filed on 10/14/2008 has been considered.

Claim Objections

Claims 10-14 and 20 are objected to because of the following informalities:

Claims 10-14 are objected for reciting non-elected sequences (e.g., SEQ ID NO: 1-2, 4-17, 18). Applicant would need to delete a non-elected subject matter at the time of allowance.

The examiner suggests that the syntax of claim 14 can be improved by placing the SEQ ID NO: 3 after the recited sequence (e.g., AVWKDFLKNIGKAAGKAVLNSVTDMVNE (SEQ ID No. 3)).

Claim 20 is objected for missing an article before the term "native amino acid" in line 2, which should either be amended to "the native amino acid to be modified" or "a native amino acid"

Appropriate correction is required.

Claim Rejections - 35 USC § 112-*written description*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-14, 20-23 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth a peptide of SEQ ID NO: 3, as stimulator of insulin secretion, and therefore the written description is not commensurate in scope with "any peptide or fragments thereof having at least 50%, 80%, 90% or 95%

sequence identity to the peptide of SEQ ID NO: 3 as stimulator of insulin secretion or pancreatic beta cell function".

The claims broadly encompass a genus of peptides that may have substitutions, deletions or insertion to replace up to 50% amino acid residues of SEQ ID NO: 3. The claims do not require that peptides or fragments thereof possess any particular feature or structure. Therefore, the claims are drawn to a genus of "any peptide or fragments thereof with 5%, 10%, 20% or up to 50% amino acid residues different from the peptide of SEQ ID NO: 3".

The specification on pg. 3, discloses an alignment of peptides isolated from different frog skin. Applicants tested these peptides in vitro using BRIN-BD11 cells for insulin secretion. The alignment of these sequences does not disclose any conserved residue or domain which could be responsible for stimulating insulin secretion. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. Some of the factual considerations that are weighed when determining a written description include the level of skill and knowledge in the art, the disclosure of complete or partial structures, the disclosure of physical and or chemical properties, adequate disclosure of the functional characteristics, the correlation between structure and function, and disclosure of methods of making.

In the instant case, the specification (on page 4-6) discloses obtaining skin secretions from frogs and testing partially purified peptide preparations for insulin secretion using rat insulin secreting cells BRIN-BD11. The specification does not

describe any peptide fragment for example, a peptide fragment of 2, 3, 4, 5 or 6 amino acids from the peptide of SEQ ID NO: 3, or a peptide having only 50% variant with the amino acid sequence of SEQ ID NO: 3 that can stimulate insulin secretion and stimulate pancreatic beta cell function. The specification does not disclose any other pancreatic beta cell function except that it produces insulin which can be used to correlate with the instant invention. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is *whatever is now claimed* (see page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (see Vas-Cath at page 1116).

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly & Co., 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In Regents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic

statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B (1), the court states an adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.

As discussed above, the skilled artisan cannot envision the detailed genus of "any peptide having at least 50%, 80%, 90% or 95% sequence identity to the peptide of SEQ ID NO: 3 or a fragment thereof" and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of making the invention. The compound itself is required. See Fiers v.Revel, 25USPQ2d 1601 at 1606 (CAFC 1993) and Amgen v.Baird, 30 Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 148 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class.

Therefore, only a peptide of SEQ ID NO: 3, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112-*scope of enablement*

Claims 10-14, 20-23 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated peptide of SEQ ID NO: 3 as stimulator of insulin secretion, does not reasonably provide enablement for any peptide having at least 50%, 80%, 90% or 95% sequence identity to the peptide of SEQ ID NO: 3 or a fragment thereof as stimulator of insulin and pancreatic beta function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to which the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include: (1) Nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the breath of the claims, (7) the quantity of experimentation needed, (8) relative skill of those in the art.

The instant disclosure fails to meet the enablement requirement for the following reasons:

The instant claims are broadly drawn to any peptide or fragment thereof having at least 50%, 80%, 90% or 95% sequence identity to the peptide of SEQ ID NO: 3 as stimulator of insulin secretion and pancreatic beta cell function.

The problem of predicting peptide structural determinations from an amino acid sequence to ascertain functional aspects of the peptide is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be

made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the peptide which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. The specification does not teach which amino acid positions are important for a peptide of SEQ ID NO: 3 in order to stimulate insulin secretion and pancreatic beta function. The specification does not disclose any peptide fragment of 2, 3, 4, 5, 6, or even 11 amino acids in length which can predictably stimulate insulin secretion and pancreatic beta cell function. Additionally, the specification does not disclose what Applicants mean by "pancreatic beta cell function" except that beta cell produces insulin. Further, because of lack of guidance and working example it would be unpredictable to one of the skill in the art how to practice the claimed invention.

Due to the large amount of experimentation necessary to make and use numerous variants of the polypeptide of SEQ ID NO: 3 having at least 50%, 80%, 90% or 95% sequence identity or a fragment thereof as stimulator of insulin secretion and pancreatic beta cell function, the lack of direction/guidance presented in the

specification regarding the same, the absence of working examples directed to same, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Charpentier et al (J. Biol. Chem. 273: 14690-14697, 1998).

The instant claim is broadly drawn to a peptide or fragment thereof having at least 50% sequence identity to the peptide of SEQ ID NO: 3 as stimulator of insulin secretion and pancreatic beta cell function.

Charpentier et al teach a peptide dermaseptine B3 precursor isolated from a frog skin. The amino acids 46-71 of the peptide dermaseptine B3 has at least 50% sequence homology with the amino acids 1-26 of the instantly claimed peptide of SEQ ID NO: 3 (see – the attached sequence alignment). Though Charpentier et al do not teach that the peptide dermaseptine B3 stimulates insulin, because the peptide has at least 50% sequence homology with the instantly claimed protein, the prior art inherently anticipates the instantly claimed invention.

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RESULT 1
T10456
dermaseptine B3 precursor - two-colored leaf frog
C;Species: Phyllomedusa bicolor (two-colored leaf frog)
C;Date: 16-Jul-1999 #sequence_revision 16-Jul-1999 #text_change 09-Jul-2004
C;Accession: T10456
R;Charpentier, S.; Amiche, M.; Mester, J.; Vouille, V.; Le Caer, J.P.; Nicolas, P.; Delfour, A.
J. Biol. Chem. 273, 14690-14697, 1998
A;Title: Structure, synthesis, and molecular cloning of dermaseptins B, a family of skin peptide antibiotics.
A;Reference number: Z17027; MUID:98278974; PMID:9614066
A;Accession: T10456
A;Status: preliminary; translated from GB/EMBL/DDBJ
A;Molecule type: mRNA
A;Residues: 1-74 <CHA>
A;Cross-references: UNIPROT:P81485; UNIPARC:UPI00001294F5; EMBL:Y16564; NID:g3256036; PIDN:CAA76288.1; PID:g3256037
C;Superfamily: dermaseptin precursor; dermorphin precursor amino-terminal homology
F;1-22/Domain: signal sequence #status predicted <SIG>
F;23-74/Product: dermaseptine B3 #status predicted <MAT>

  Query Match             51.4%;  Score 73;  DB 2;  Length 74;
  Best Local Similarity   53.8%;  Pred. No. 0.0027;
  Matches   14;  Conservative    5;  Mismatches    7;  Indels    0;  Gaps    0;

Qy          1 AVWKDFLKNIGKLAGKAVLNSVTDMV 26
              :|:|: || ||| |:|: | :|  :|
Db         46 ALWKNMLKGIGKLAGQAALGAVKTLV 71
```

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GYAN CHANDRA whose telephone number is (571)272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Robert Landsman/
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